REMARKS

Drawings

The drawings were objected to under 37 CFR 1.83(a) because it allegedly "fail to show the washer (140) as described in the specification." *Office Action* at 2. As directed by the Office, a proposed drawing correction is submitted herewith. FIG. 1 has been amended to indicate a washer 140. The amendment has been made in red ink to clearly depict the proposed drawing correction. If the Office finds the proposed drawing correction acceptable, Applicants will submit a new formal FIG. 1 upon receipt of a Notice of Allowance.

Cancellation of Claims

Claims 6, 9, 14, and 34 are canceled herein without prejudice, waiver, or disclaimer. Applicants take this action merely to reduce the number of disputed issues and to facilitate early allowance and issuance of other claims in the present application. Applicants reserve the right to pursue the subject matter of those canceled claims in a continuing application, if Applicants so choose, and do not intend to dedicate any of the canceled subject matter to the public.

Response To Objections/Rejections

Response To Double Patenting Rejection

Claims 1-9 and 14 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 25-28 of copending Application No 09/773,826. Specifically, the Office states:

> Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application recite a system comprising a filter vessel, wherein an incubator, sample separation system, image acquisition system, and robotic pipettor are separately recited in dependent claims. The independent claim of the '826 application recites all of the separate components together. The instant application is broader in all respects than the claims of the '826 application and thus, the instant application anticipates the

> claims of the '826 application. See In Re Goodman, 11 F.3d 1046, 29 USPQ32d 2010 (Fed. Cir. 1993).
>
> This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Office Action at 6-7. Applicants respectfully traverse.

Nevertheless, to advance prosecution and facilitate early allowance of the claims, Applicants submit herewith a terminal disclaimer pursuant to 37 C.F.R. §1.321(c). Applicants have submitted the terminal disclaimer solely to advance prosecution of the application, without conceding that the double patenting rejection is properly based. In filing the terminal disclaimer, Applicants rely upon the rulings of the Federal Circuit that the filing of such a terminal disclaimer does not act as an admission, acquiescence or estoppel on the merits of the obviousness issue. *See, e.g., Quad Environmental Tech v. Union Sanitary Dist.*, 946 F.2d 870, 874-875 (Fed. Cir. 1991); and *Ortho Pharmaceutical Corp. v. Smith*, 959 F.2d 936, 941-942 (Fed. Cir. 1992).

Response To Claim Rejections Under 35 U.S.C. §102

(a) Claims 1-5, 8, 10-12, 23-31, 35, and 36-38 are rejected to under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,620,898 to *Yaremko et al.* Specifically, the Office Action states:

> Yaremko et al teach an automated blood analysis system. The system comprises a microcolumn (122), incubator (200), centrifuge (500), pipette assembly (400), washer (406, 410) and imaging system (606), as recited in claims 1-5. The incubator holds containers/receptacles while reagents and fluids are being dispensed into the containers and incubates the containers (col. 5, lines 39-42). The containers/ receptacles are microcolumns having a filter through which the assay sample travels. The filters provide an irregular "bottom" for the vessel, as recited in claim 1. The centrifuge rotates the containers within it (containing the assay sample) to push the cellular material in the sample through the filter material and thus separate the sample, as recited in claims 3, 8, 11 and 12 (col. 13, line 61 - col. 15, line 3).
>
> At col. 14, line 61 to col. 15, line 3, the reference teaches centrifuging at a lower speed to push the cells toward the filter and to increase cell to cell contact to achieve maximum reactivity, as recited in claims 24-26, 35, 36 and 38. The imaging system comprises a camera (644) for capturing an image of the analysis

> of the sample, as recited in claim 4 (col. 15, line 48 – col. 16, line 21). The pipette assembly comprises a pipette (402) and a robot arm (404), as recited in claim 5 (col. 13, lines 1-12). Yaremko et al teach that the system is used for analyzing blood samples and for identifying antibodies and antigens as recited in claim 10.
>
> With respect to the method of claims 23, 28 and 29, Yaremko et al teach providing a filter vessel; adding a blood sample and reagent to the vessel, centrifuging the vessel and analyzing the centrifuged components. With respect to claim 31, Yaremko et al. teach that the filter in the microcolumn may be a porous gel material (col. 6, lines 21-32).

Office Action at 2-3. Applicants respectfully traverse. For a proper rejection of a claim under 35 U.S.C. Section 102(b), the cited reference must disclose all elements/features of the claim. *See, e.g., E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co.*, 849 F.2d 1430, 7 USPQ2d 1129 (Fed. Cir. 1988).

Yaremko et al. do not disclose, teach, or suggest all of the claimed elements. For example, *Yaremko et al.* do not disclose, teach, or suggest the feature of "a vessel comprising a bottom with an uneven surface," as recited in claim 1 or "a vessel having a bottom with an uneven surface," as recited in claim 23. The microbeads recited in *Yaremko et al.* are "deposited in" the microcolumns, and thus are not an integral part of the vessel. Thus, independent claims 1 and 23 are allowable over *Yaremko et al.*

Nevertheless, to advance the prosecution and facilitate allowance of the claims, Applicants have amended claims 1 and 23 to include the features of their respective dependent claims 9 and 34, *i.e.*, a flow cytometer. Dependent claims 9 and 34 were not rejected based on allegedly being anticipated by *Yaremko et al.* Thus, incorporation of these features into independent claims 1 and 25 should obviate the rejection.

Thus, *Yaremko et al.* does not anticipate amended claims 1 and 23, and Applicants respectfully request that the rejection be withdrawn.

If independent claims 1 and 23 are allowable over the prior art of record, then their dependent claims 2-5, 8, 10-12, 24-31, 35, and 36-38 are also allowable as a matter of law, because these dependent claims contain all features/elements/steps of their respective independent claims. *See Minnesota Mining and Mfg. Co. v. Chemque, Inc.*, 303 F.3d 1294, 1299 (Fed. Cir. 2002). Additionally and notwithstanding the foregoing reasons for the allowability of claims 1 and

23, these dependent claims recite further features and/or combinations of features (as is apparent by examination of the claims themselves) that are patentably distinct from the prior art of record. Hence, there are other reasons why these dependent claims are allowable.

(b) Claims 1, 6, 7, 9, 13-16, 18-22, and 39-45 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,692,702 to *Burshteyn et al.* In particular, the Office Action states:

> Burshteyn et al. teach an apparatus for biological sample preparation and analysis, specifically blood cell analysis. The apparatus of Burshteyn et al. comprises sample filter vessel (24). The filter vessel comprises a microporous hollow fiber membrane having a plurality of pores. The porous filter allows the vessel to have an irregular bottom. The porous membrane may be a nylon membrane, having a pore size of -0.1-5 microns, as recited in claims 6 and 7 (col. 7, lines 43-59). At col. 15, lines 55-59, Burshteyn et al. teach that a vacuum forces [sic] causes components of the blood to pass through the filter while retaining cells of interest, as recited in claim 16. A fluorescently-labeled antibody (reagent) is added to the blood sample to form a test mixtures [sic], as recited in claims 15 and 19-22. The test mixture is analyzed with a flow cytometer to quantitatively measure the amount of antigen-specific antibody associated with each cell in the test sample as recited in claims 9, 13, 14 (col. 16, lines 44-52).

Office Action at 3-4. Applicants respectfully traverse. Nevertheless, Applicants need not address the Examiner's substantive arguments because the element of 102(e) has not been met that "the invention was described in ... (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent...." *35 U.S.C. 102(e)* (emphasis added). Applicant's date of invention precedes the filing date of the *Burshteyn et al.* reference.

Applicants' instant application ultimately claims priority to Applicants' provisional U.S. patent application serial no. 60/179,248, filed on January 31, 2000 ("Applicants' '248 Application"). The *Burshteyn et al.* reference was filed on July 7, 2000. Therefore, Applicants' date of invention predates the filing date of the *Burshteyn et al.* reference. Support for Applicants' claims 1, 15, and 39, in the least, can be found in Applicants' '248 Application at pages 3-5 and 10-11. Because the *Burshteyn et al.* reference was not filed before the invention thereof by the Applicants, Applicants respectfully request that the rejection of claims 1, 15, and 39 be withdrawn.

If independent claims 1, 15, and 39 are allowable over the prior art of record, then their dependent claims 6, 7, 9, 13-14, 16, 18-22, and 40-45 are also allowable as a matter of law, because these dependent claims contain all features/elements/steps of their respective independent claims. There may be other reasons why these dependent claims are allowable.

Response To Claim Rejections Under 35 U.S.C. §103

(a) Claims 15, 17-22, 34, and 39-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Yaremko et al.* in view of U.S. Patent No. 5,968,731 to *Layne et al.* Specifically, the Office Action states:

> The disclosure of *Yaremko et al.* is described above. *Yaremko et al.* fail to teach a flow cytometer in the system for image acquisitioning.
>
> *Layne et al.* is directed to an apparatus for automated testing of biological specimens *Layne et al.* teach that image acquisitioning in automated analyses allows detection of target individual cells and allows the collection of data to be observed by the user later. *Layne et al.* teach that flow cytometry is suitable for image acquisition (col. 14, lines 14-19; col. 17, lines 34-39). It would have been obvious to one of ordinary skill in the art to modify the *Yaremko et al.* reference by substituting the camera imaging system for a flow cytometry imaging system, as taught by *Layne et al.* In testing of blood specimens, such a modification would allow the user to detect and analyze individual blood cells.

Office Action at 5. Applicants respectfully traverse. It is well established at law that, for a proper rejection of a claim under 35 U.S.C. §103 as being obvious based upon a combination of references, the cited combination of references must disclose, teach, or suggest, either implicitly or explicitly, all elements/features/steps of the claim at issue. See, *e.g.*, *In Re Dow Chemical*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988), and *In re Keller*, 208 U.S.P.Q. 871, 881 (C.C.P.A. 1981).

The combination of *Yaremko et al.* with *Layne et al.* do not teach or suggest the features of claim 34. It should be noted that claim 34 has been cancelled; however, its subject matter, as noted previously, has been incorporated into their respective independent claims 1, 15, 23, and 39. Thus, Applicants now make their arguments with respect to the claimed subject matter of newly amended claims 1, 15, 23, and 39.

The combination of *Yaremko et al.* with *Layne et al.* does not teach or suggest the features of independent claims 1, 15, 23, and 39. Amended claims 1 and 15 both include the language: "wherein the image acquisition system consists of a flow cytometer or a capillary cytometer." Amended claim 23 recites the following: "wherein the interactions are evidenced by agglutination, and wherein the interactions are analyzed via a flow cytometer or a capillary cytometer." Amended claim 39 recites the following: "determining the presence of agglutination with the flow cytometry."

As admitted by the Office, *Yaremko et al.* failed to teach a flow cytometer as an imaging acquisition system. *Layne et al.* also do not cure this deficiency of *Yaremko et al.*

When describing their image acquisition apparatus at column 14, lines 14-19, *Layne et al.* simply disclose that "the image acquisition and analysis SLM 224 detects individual HIV-infected cells within cell monolayers, and collects observable data. In one embodiment, the image acquisition and analysis SLM comprises a digital image analysis system **and** motorized microscope stages ...." *Layne et al.* at col. 14, lines 14-19 (emphasis added). *Layne et al.* couple their digital image analysis system with motorized microscope stages. Nowhere in the specification do *Layne et al.* teach that its digital image analysis system is in fact composed only of a flow cytometer.

With respect to the claim language of *Layne et al.* that includes a flow cytometer, the claim language reads as follows: "multiple detector instruments which are selected for the same biological specimen, in which are at least two of a digitized microscope, a colorimeter, a flow cytometer, and a scintillation detector." *Layne et al.* at claims 12 and 23 (emphasis added). Again, *Layne et al.* require, in addition to the flow cytometer, another type of detector instrument to analyze the biological specimen as part of its image acquisition system.

Claims 1 and 15 have been amended herein to recite "wherein the image acquisition system consists of a flow cytometer or a capillary cytometer." (Emphasis added). By using the closed expression "consists of", Applicants submit that the image acquisition system of claim 1 excludes the combination digital analysis system of *Layne et al.* Even though the preamble recites the "comprising" language, and therefore additional elements can be included in the immunological assay system, because Applicants have used the "consisting of" language for the image acquisition system, any additional elements within the immunological assay system cannot

therefore be part of the image acquisition system. Because *Layne et al.* specifically recite multiple detector instruments as a requirement of their image acquisition system, and not solely the cytometer, *Layne et al.* do not render the present claims 1 and 15 obvious.

Similarly, for claims 23 and 39, as noted above, amended claim 23 recites "wherein the interactions are evidenced by agglutination, and wherein the interactions are analyzed via a flow cytometer or a capillary cytometer." Amended claim 39 recites "determining the presence of agglutination with the flow cytometry." *Layne et al.* do not teach or suggest that a flow cytometer can be used to analyze or determine the presence of agglutinations. Therefore, for at least this reason, *Yaremko et al.* in view of *Layne et al.* do not render claims 1, 15, 23, and 39 obvious. Applicants therefore respectfully request that the rejection of claims 1, 15, and 39 be withdrawn.

Furthermore, *Yaremko et al.* in view of *Layne et al.* do not teach or suggest at least the features of claims 1 and 15 of "the vessel comprises a filter material chosen from at least one of the following: a polypropylene; a cellulose nitrate; a nylon; polyvinylidene fluoride; and HPVM membrane," or the feature of claim 32 of "wherein the filter comprises a material selected from a polypropylene, a nylon, a cellulose nitrate and polyvinylidene fluoride," or the features of claim 39 of "a vessel with an uneven bottom surface, wherein the bottom of the vessel comprises a filter material chosen from at least one of the following: polypropylene, cellulose nitrate, nylon, polyvinylidene fluoride, and HPVM membrane." *Yaremko et al.* teach the following:

> A multitude of very small, transparent glass beads, having diameters on the order of magnitude of 10 to 100 micrometers, are deposited in and form a filter in the lower portion of each microcolumn. Alternately, the lower portion of each microcolumn may be provided with a suitable gel that functions in the same general way as the microbeads.

Yaremko et al. Thus, *Yaremko et al.* do not teach or suggest the features of the filter vessel noted above. Moreover, *Layne et al.* do not cure this deficiency. No where do *Layne et al.* teach the features of the filter vessels recited above of claims 1, 14, 32, and 39.

As noted in the specification as originally-filed:

> When antibodies and RBCs are reacted in the well, and then centrifuged, the irregular topography of the well bottom impedes RBC rolling and movement, causing the RBCs to spread evenly over the bottom. In contrast, if the vessel has a

> smooth bottom, such as a standard 96-well plastic assay plate without filter material at the bottom, the force of centrifugation may cause all of the RBCs to roll along the smooth bottom and localize into a corner of the vessel. In the presence of antibodies that bind RBCs, the tightly packed RBCs in a smooth-bottomed plate can form large agglutinates or aggregates, while in plates with irregular bottom topography the dispersed RBCs either remain as single cells or form only very small agglutinates. When the samples are analyzed using a flow cytometer as the image acquisition system, the individual cells and small agglutinates formed in plates with irregular bottom topography can be readily and accurately analyzed.

Specification at page 7, line 22 - page 8, line 2. These are surprising, nonobvious results in view of *Yaremko et al* and *Layne et al.* Thus, for at least these reasons as well, the rejection of claims 1 (and its dependent claims), 15 (and its dependent claims), 32, and 39 (and its dependent claims) should be withdrawn.

In addition to the differences discussed above, the configuration of the flow cytometer recited in claims 1, 15, 23, and 39 is not taught or suggested by the prior art. Flow cytometers are automated instruments that traditionally have been used to measure properties of single cells, one cell at a time. Even *Layne et al.* teaches that "[t]he image acquisition and analysis SLM 224 detects individual HIV-infected cells within cell monolayers...." *Layne et al.* at col. 14, lines 14-15. (emphasis added). In contrast, claim 1 recites the following: "wherein the image acquisition system designed to detect the presence of interactions between the components in the assay sample and the reagent, wherein said interactions are evidenced by agglutination, wherein the image acquisition system is composed of a flow cytometer or a capillary cytometer." *Claim 1*, as amended (emphasis added). Thus, the flow cytometer as recited in claim 1 does not necessarily require single cells, but rather is being used to detect agglutinations of cells.

Similarly, claim 15 recites the following: "wherein the cytometer is designed to detect the presence of interactions between components in the assay sample and the reagent, wherein the interactions are evidenced by agglutination." Claim 23 recites "wherein the interactions are evidenced by agglutination, and wherein the interactions are analyzed via a flow cytometer or a capillary cytometer." Claim 39 recites "determining the presence of agglutination with the flow cytometry." Each of these claims recite in some form the feature of the flow cytometer measuring agglutinations.

With respect to claims 1 and 15, Applicants note in particular that the "designed to" language in amended independent claims 1 and15 is not merely functional language, but should be construed as a structural feature of the systems of claims 1 and 15. *See* MPEP 2173.05(g), last paragraph ("[T]he Court held that limitations such as 'members adapted to be positioned'... serve to precisely define present structural attributes of interrelated component parts of the claimed assembly. *In re Venezia*, 530 F.2d 956, 189 USPQ 149 (CCPA 1976)." (emphasis added)). Applicants submit that the feature of claim 1 of "wherein the image acquisition system is designed to detect the presence of interactions," and the feature of claim 15 "designed to detect the presence of interactions," precisely define structural attributes of the flow cytometer and are not merely functional language.

Because the combination of *Yaremko et al.* in view of *Layne et al.* do not render claims 1, 15, 23, and 39 obvious, Applicants respectfully request that the rejection be withdrawn.

If independent claims 1, 15, 23, and 39 are allowable over the prior art of record, then their dependent claims 17-22, 34, and 40-46 are also allowable as a matter of law, because these dependent claims contain all features/elements/steps of their respective independent claims. There may be other reasons why these dependent claims are allowable.

(b) Claims 32-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Yaremko et al.* in view of U.S. Patent No. 6,008,040 to *Datar*. Specifically, the Office Action states:

> The disclosure of Yaremko et al. is described above. Yaremko et al. fail to teach the particular filter materials recited in claim 32-33.
>
> Datar teaches efficient separation of cells, cellular materials and proteins. Specifically, Datar teaches separation devices such as bead columns. Further, Datar teaches that cellulose acetate beads, polyesters, and nylons are suitable for use in separation columns due to their specific chemistries on their contacting surfaces (col. 4, lines 24-41). It would have been obvious to one of ordinary skill in the art to use filter materials, such as cellulose acetates, polyesters, and nylons as the filter material in the microcolumn of Yaremko et al. These materials are known to be suitable in the separation of cellular material. The ordinarily-skilled artisan would have expected that these filter materials would perform sufficiently in separating blood cells.

Office Action at 5. Applicants respectfully traverse on the grounds that *Yaremko et al.* in view of *Datar* do not teach or suggest all of the features of claim 32-33.

As noted above, *Yaremko et al.* do not teach or suggest the filter vessel material of claims 32 and 33. Moreover, *Datar et al.* do not cure these deficiencies of Yaremko et al. Specfically, as the Examiner notes, *Datar et al.* teach use the filter material in their separation columns "in the *separation* of cellular material. The ordinarily-skilled artisan would have expected that these filter materials *would perform sufficiently in separating blood cells.*" *Office Action* at 5 (emphasis added). As noted above, the filter materials of claims 32 and 33 are not used for their separation characteristics, but rather to spread out the reaction materials over the bottom surface of the vessel for cytometric analysis. This is nonobvious in view of *Datar et al.* and Applicants respectfully submit that for at least this reason, the rejection of claims 32 and 33 should be withdrawn.

In addition, because claims 32-33 depend from allowable amended claim 23 (as argued herein), claims 32-33 should also be allowable. Applicants respectfully request that the rejection be withdrawn.